1070-36 Plasma Brain Natriuretic Peptide Levels Increase in Proportion to the Extent of Right Ventricular Dysfunction in Pulmonary Hypertension

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Background: Plasma BNP is known to increase in proportion to the degree of left ventricular (LV) overload. However, whether brain natriuretic peptide (BNP) secretion is also regulated in the presence of right ventricular (RV) overload remains unknown. This study sought to investigate the influence of RV hemodynamics and function on the secretion of BNP in patients with isolated RV overload.

Methods: Plasma BNP and atrial natriuretic peptide (ANP) levels in the pulmonary artery were measured in 44 patients with RV overload: RV volume overload (RVVO) due to atrial septal defect (n = 18) and RV pressure overload (RVPO) due to primary or thromboembolic pulmonary hypertension (n = 26). Right heart catheterization was performed in all patients. RV and LV ejection fraction, myocardial mass, and volume of the 4 chambers were determined using electron beam computed tomography.

Results: Though both plasma BNP and ANP were significantly elevated in RV overload compared with control subjects, plasma BNP and BNP/ANP ratio were significantly higher in RVPO than in RVVO (BNP: 294 ± 72 vs. 48 ± 14 pg/ml, BNP/ANP: 1.6 ± 0.2 vs. 0.8 ± 0.2, $p < 0.05$, respectively). Plasma BNP positively correlated with mean pulmonary arterial pressure (r = 0.73), total pulmonary resistance (r = 0.79), mean right atrial pressure (r = 0.79), RV end-diastolic pressure (r = 0.76), and RV myocardial mass (r = 0.71); negatively correlated with cardiac output (r = 0.33) and RV ejection fraction (r = 0.71). Plasma BNP significantly decreased from 315 ± 120 to 144 ± 54 pg/ml by long term vasodilator therapy (total pulmonary resistance decreased from 23 ± 4 to 15 ± 3 Wood units).

Conclusions: Plasma BNP levels increase in proportion to the extent of RV dysfunction in pulmonary hypertension.

1070-37 Therapeutic Effects and Limitation of Human Atrial Natriuretic Peptide in Patients With Congestive Heart Failure

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Background: Alpha human atrial natriuretic peptide (ANP) is available as a therapeutic agent for congestive heart failure. Continuous administration of ANP has been reported to induce the attenuation of hemodynamic effects in patients with congestive heart failure due to dounregulation of ANP receptors. This study was designed to elucidate the relationship between levels of endogenous ANP and therapeutic effects of exogenous ANP.

Methods: Fourteen patients with congestive heart failure were divided into two groups on the basis of baseline level of endogenous ANP (pg/ml) (high group: ≥250, n = 7; low group: <250, n = 7). After baseline measurements were obtained, dose titration was started by infusing ANP at a rate of 0.05 μg/kg/min. After achieving the desired hemodynamic response (30% reduction of pulmonary artery pressure), the infusion rate of ANP was maintained for 24 hours. Measurements of hemodynamic parameters and blood sampling were performed serially at the baseline, 6, 12, 18, and 24 hours after the infusion.

Results: At the baseline, mean pulmonary artery pressure (PA, mmHg), mean pulmonary capillary wedge pressure (PCWP, mmHg), and plasma cGMP level were comparable in the two groups. At 6 hours after the infusion of ANP, PA and PCWP were significantly decreased (high group: PA, 47 ± 6 to 33 ± 5; PCWP, 23 ± 6 to 15 ± 4; low group, PA: 45 ± 8 to 32 ± 6; PCWP: 24 ± 8 to 16 ± 5), and plasma cGMP (pmol/ml) was significantly increased (high group, 8 ± 3 to 39 ± 11; low group, 3 ± 2 to 44 ± 13). However, at 12 hours, in the high group, PA (39 ± 11) and PCWP (21 ± 5) were significantly elevated ($p < 0.05$ vs at 6 hours) and plasma cGMP (14 ± 6) was significantly decreased ($p < 0.05$ vs at 6 hours). In contrast, in the low group, the effects on PA (29 ± 5), PCWP (17 ± 4) and plasma cGMP (39 ± 11) were maintained at 12 hours.

Conclusion: ANP is a potentially useful therapeutic agent for congestive heart failure in patients with low level of endogenous ANP. But the effects may be attenuated in patients with high level of endogenous ANP during continuous administration of ANP.

1070-38 Infusion or Co-infusion of Brain Natriuretic Peptide And/or Adrenomedullin in Human Heart Failure

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In random order, placebo controlled, studies we gave 4 hour (h) infusions of Brain Natriuretic Peptide (B) (3.0 pmol/kg/min), Adrenomedullin (A) (2.65 and 5.3 pmol/kg/min; 2 h each) or both combined (C) to 6 males with congestive heart failure (CHF, left ventricular ejection fractions <35%). Blood pressure (BP) fell with B, A and C (peak falls: systolic 10, 20 and 23 mmHg and diastolic 8, 17, 19 mmHg respectively, $p < 0.01$ for all). Heart rate increased with A and C (peak increase 13 bpm for both, $p < 0.01$). Plasma B increased with B and C (peak increase 60pmol/L for both, $p < 0.01$). A was increased by A and C (peak increase 60 pmol/L for both, $p < 0.01$). Atrial natriuretic peptide, epinephrine and cortisol were unchanged. Norepinephrine (NE) was increased by B, A and C (peak rise 650, 1163, and 1403 pmol/l respectively, i.e. by 31–66%, $p < 0.01$). Renin was unchanged by B but increased by A and C (peak rise 320 and 290%, $p < 0.01$) whilst aldosterone was similar on each day. Sodium excretion increased with B and C (peak increase 12.8 and 10.9 mmol/4 hrs respectively, $p < 0.05$ for both). A, B and C infusions caused significant decreases in BP (the greatest with A and C). Increases in heart rate, NE and renin occurred during A and C infusions, but only NE rose with B. The expected aldosterone response to major increases in renin was blocked by A. B (but not A) had a significant natriuretic effect which was preserved with C despite a marked fall in BP. Co-augmentation of Brain Natriuretic Peptide and Adrenomedullin systems has unique hemodynamic effects in human CHF.

1070-39 Enhancement of Renal 11-β-Hydroxysteroid Dehydrogenase Activity in Chronic Heart Failure and Essential Hypertension Treated With ACE-Inhibition

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Background: ACE-inhibition is a current treatment for both chronic heart failure (CHF) and essential hypertension (EHT). Steroid metabolism is known to be interfered with by chronic ACE-inhibition and may lead to the so called steroid escape phenomenon. We tested the hypothesis whether chronic ACE-inhibition differently influences cortisone/cortisol excretion due to activation of renal 11-β hydroxysteroid dehydrogenase.

Methods: Thirteen patients (71 ± 6 years) with chronic heart failure (CHF, NYHA class II, ejection fraction 32 ± 13%) under a stable therapy with captopril 100 mg/d and furosomide 40 mg/d were examined together with 7 patients (61 ± 6 years) with essential hypertension (EHT) treated with captopril 50 mg/d for at least 3 months. 24 Hours urine (U) was collected for the determination of cortisone (1) and cortisol (2) metabolites and their ratio using HPLC chromatography as well as blood sampling for the renin-angiotensin-aldosterone system in supine position.

Results:

Plasma	CHF	EHT	
Renin (μU/ml)	951 ± 1479	120 ± 117	P < 0.001
Angiotensin II (pg/ml)	34.2 ± 27.7	21.1 ± 11.4	P < 0.01
Aldosterone (ng/dl)	18.0 ± 13.4	11.2 ± 9.1	P < 0.05
U-cortisone (1) (μg/24 h)	64 ± 36	39 ± 25	P < 0.01
U-cortisol (2) (μg/24 h)	33 ± 21	30 ± 19	NS
(1)/(2) ratio	2.10 ± 0.76	1.51 ± 1.16	P < 0.05

Conclusions: In essential hypertension and chronic heart failure under chronic ACE-inhibition there is a steroid escape phenomenon which is significantly greater in the heart failure process. The higher cortisone/cortisol ratio in chronic heart failure under ACE-inhibition suggests a more enhanced renal 11-β hydroxysteroid dehydrogenase activity in chronic heart failure.

1070-40 Angiotensin Converting Enzyme Deletion Polymorphism Does Not Increase the Risk of Heart Failure

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Background: The role of the deletion allele of the angiotensin converting enzyme (ACE "D") as a risk factor for the development congestive heart failure remains controversial. In this case control study we sought to evaluate the hypothesis that the deletion allele would be increased in prevalence in a heart failure population, when compared to age matched controls.

Methods: DNA was isolated from whole blood and ACE genotyping performed on a series of 212 patients (P) with congestive heart failure referred to the Heart Failure service at the University of Pittsburgh (M/F 160/52, age = 55.3 ± 7 11.4). These were compared to a series of 124 controls (C) without any history of heart failure or coronary disease (M/F 74/50 age = 54.7 ± 10.2)

Results: The frequency of homozygotes for the insertion allele (II), heterozygotes (ID), or homozygotes for the deletion allele (DD), did not differ between patients and controls as is displayed by the table below.

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